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54 Microbiocidal agents

Described are microbiocidal agents containing toxicologically safe, low-odor or odor-free organic acids and alkyl sulfonates and/or alkyl sulfates as active substances. Whereas the individual components have no microbiocidal activity in the concentrations used, the combinations thereof have surprisingly shown bactericidal, fungicidal, and virucidal activity.

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Microbiocidal Agents

Claims

1. Microbiocidal agents, characterized by a content of organic acids and secondary and/or primary alkyl sulfonates and/or alkyl sulfates containing 8 to 18 carbon atoms in the alkyl group, the cation of which is derived from alkali metals, amines, or ammonium groups.

2. Microbiocidal agents according to Claim 1, characterized in that the alkyl sulfonates and alkyl sulfates contain 10 to 16, in particular 12 to 14, carbon atoms.

3. Microbiocidal agents according to Claims 1 and 2, characterized in that the organic acids comprise

aliphatic, aromatic, or heterocyclic carboxylic acids, which may be substituted or unsubstituted and contain up to 4 carboxyl groups, in addition to CH- or NH-acid compounds, and mixtures of these acids.

4. Microbiocidal agents according to Claims 1 through 3, characterized in that the aliphatic carboxylic acids are saturated or unsaturated, straight-chain or branched, or cyclic, and contain up to 12 carbon atoms.

5. Microbiocidal agents according to Claims 1 through 4, characterized in that the organic acids have a pK_a value of 2 to 6.

6. Microbiocidal agents according to Claims 1 through 5, characterized in that the organic acids comprise tartaric acid, benzoic acid, substituted benzoic acids, or mixtures thereof.

7. Microbiocidal agents according to Claims 1 through 6, characterized in that the weight ratio of alkyl sulfonate and/or alkyl sulfate to organic acids is between 50:1 and 1:50, preferably between 9:1 and 1:9, particularly preferably between 9:1 and 1:1.

8. Microbiocidal agents according to Claims 1 through 7, characterized in that said microbiocidal agents contain monohydric or polyhydric lower aliphatic alcohols for dissolving insoluble acids.

9. Microbiocidal agents according to Claims 1 through 8, characterized in that the pH of the stock solution is between 0.1 and 5, in particular between 2 and 4.

Description

An increasingly pressing need expressed by leading hygienists is a fast-acting disinfectant having a broad activity spectrum, but whose active ingredients have no adverse toxicological effects, thereby ensuring problem-free use in food hygiene. Disinfection in food operations is much more difficult than in the medical field, since the number of chemicals that may be considered is greatly limited. Highly odorous or toxic products are excluded from the outset. These include aldehydes, which, although such compounds have a broad activity spectrum, they cannot be used on account of their odor characteristics and allergic effect. In addition, aldehydes have a soap interference effect, and their effectiveness is greatly reduced at temperatures below 18°C. Phenols, which are some of the oldest disinfectants, are also odorous and toxic. Peracids, halogens, and halogen-cleaving compounds also emit an unpleasant odor. Other known disinfectants such as quaternary ammonium salts have large discontinuities in their activity spectrum, or are inactivated to an excessive extent by protein contamination. Guanidine derivatives also have toxic effects, whereas alcohols must be used in concentrations of 60 to

80% to achieve a rapid disinfectant effect. For spraying large surface areas, such high concentrations must be avoided at all costs due to the explosion hazard.

The same requirements imposed on disinfectants for the food industry and commercial kitchens also apply to the kitchen area in households, such as sinks, work surfaces, refrigerators, and food processors, for which a bactericidal effect is to be achieved in the shortest possible time using a ready-to-use solution of very low toxicity in order to kill spoilage agents and pathogenic organisms.

Of course, a nontoxic, fast-acting disinfectant also has advantages for the fields of medicine and hygiene.

It has been found that combinations of the alkyl sulfonates and/or alkyl sulfates defined in Claim 1 with one or more organic acids in very low usage concentrations, in which the individual components of these combinations have no microbiocidal activity, have an unexpectedly broad microbiocidal

and virucidal effect with no acute toxic properties and practically no intrinsic odor. Killing *Staphylococcus aureus*, for example, within 15 minutes requires 7.5% lactic acid, whereas this effect is achieved in the same time period using a mixture of C_8–C_{18} alkyl sulfonate and lactic acid in a 4:1 ratio with a lactic acid concentration of 0.003%. Comparable values are obtained using other acids.

Thus, the minimum inhibitory concentration (MIC) for sorbic acid against *Staphylococcus aureus* is 0.7%, and against *Escherichia coli* is 0.2%. In a mixture of 4 parts C_8–C_{18} alkyl sulfonate, within 30 minutes *Staph. aureus* is killed at a sorbic acid concentration of only 0.0042%, and *E. coli* is killed at a sorbic acid concentration of 0.0150%.

For benzoic acid the MIC value against *Staph. aureus* is 0.1%, and against *E. coli*, 0.125%. In a mixture of 4 parts C_8–C_{18} alkyl sulfonate, an acid concentration of 0.0075% is sufficient to kill *Staph. aureus* within 15 minutes, and for *E. coli*, an acid concentration of 0.0300%.

Similarly, in a mixture of 4 parts C_8–C_{18} alkyl sulfonate only 0.003% citric acid is required for killing *Staph. aureus*, and for *E. coli*, only 0.010% citric acid is required, whereas the minimum inhibitory concentration of citric acid alone against these two microorganisms is significantly higher at 0.25%.

By suitable combinations of the acids used, the activity spectrum may even be extended to resistant fungi such as *Aspergillus niger*, *Aspergillus fumigatus*, and *Penicillium expansum*.

The microbiocidal agents according to the invention are active over a broad temperature range. Of particular advantage is their activity at lower temperatures, which makes them especially suited for disinfection of cold storage chambers and refrigerators.

The alkyl sulfonates and alkyl sulfates used in the microbiocidal agents according to the invention contain 8 to 18, preferably 10 to 16, in particular 12 to 14, carbon atoms in the alkyl group, which may be primary or secondary. The cation in the alkyl sulfonates and alkyl sulfates is derived from alkali metals, amines, and substituted amines, in addition to ammonium and substituted ammonium groups

such as the triethanolammonium group. Sodium alkyl sulfonates and sodium alkyl sulfates are preferred.

Considered in particular for the combination with the alkyl sulfonates and alkyl sulfates are carboxylic acids, namely aliphatic, aromatic, and heterocyclic carboxylic acids, which may contain up to 4 carboxyl groups. The aliphatic acids may be saturated or unsaturated, substituted or unsubstituted, straight-chain or branched, and also cyclic. The open aliphatic carbon chain may be interrupted by heteroatoms such as oxygen atoms. The aliphatic acids generally contain 1 to 12 carbon atoms, preferably 1 to 6 carbon atoms. Examples of such acids are formic acid, acetic acid, methoxyacetic acid, hydroxyacetic acid, lactic acid, glyoxylic acid, diglycolic acid, lauric acid, undecylenic acid, succinic acid, tartaric acid, citric acid, itaconic acid, citraconic acid, pyruvic acid, gluconic acid, sorbic acid, and aralkyl acids such as *p*-hydroxyphenylacetic acid, cyclohexanecarboxylic acid, and 2-ethylhexane carboxylic acid.

Used in particular as aromatic acids are benzoic acid and derivatives thereof, for example methylbenzoic acids, methoxybenzoic acids, salicylic acid, acetylsalicylic acid, and

multivalent aromatic carboxylic acids such as phthalic acids.

Mentioned as heterocyclic acids are furancarboxylic acids and pyridinecarboxylic acids, such as tetrahydrofurancarboxylic acid and pyridinedicarboxylic acid.

Besides carboxylic acids, sulfonic acids may also be considered as organic acids, for example alkylsulfonic acids corresponding to the alkyl sulfonates used according to the invention, cyclohexanesulfaminic acid; phosphonic acids such as 2-phosphonobutane-1,2,4-tricarboxylic acid and 1-hydroxyethane-1,1-diphosphonic acid, whereby the phosphonic acids act not only as proton donors but also as sequestering agents and corrosion inhibitors; and CH-acid compounds such as ß-ketocarboxylic acid ester, malonic acid diester, pentamethoxycarbonyl cyclopentadiene, barbituric acid, or 2,4-dioxo-3-methyltetrahydrofuran (tetrinic acid), and NH-acid compounds such as benzisothiazolone-S-dioxide.

Instead of the free organic acids, salts of these acids may also be used, such as alkali salts, which are converted to the desired free acid form by addition of an inorganic acid.

If the acids used have limited solubility in water, it is

advantageous to add alcohols such as ethanol, n-propanol and isopropanol, or 1,2-propanediol to bring the acids into solution. The alcohols also contribute to more rapid drying of the formulations.

The weight ratio of alkyl sulfonate and/or alkyl sulfate to organic acids is between 50:1 and 1:50, preferably between 9:1 and 1:9, and particularly preferably between 9:1 and 1:1. The weight ratio is determined by the pK_a value of the selected acids as well as the pH value resulting from the combination. The pH of the stock solution may be between 0.1 and 5.0. An optimal microbiocidal effect is achieved in the pH range of 2 to 4.

One or more organic acids may be used for the combination with the alkyl sulfonates and/or alkyl sulfates. Acid mixtures of aliphatic and aromatic carboxylic acids have proven to be particularly effective. By suitable selection of the acids used, particularly effective formulations may be produced, such as those with superior activity against resistant fungi, as illustrated in Example 3 in comparison to Example 2.

Besides the alkyl sulfonates and/or alkyl sulfates, the formulations according to the invention may contain

compatible surfactants, i.e., anionic, nonionic, and ampholytic-type surfactants.

In combination with sodium chloride, anionic surfactants of the fatty alcohol ether sulfate type, for example sodium lauryl myristyl ether sulfate, increase the viscosity of an aqueous solution.

Nonionic surfactants, in particular fatty alcohol polyglycol ether with a suitable ethoxylation number, may be used for foam regulation of the active substance mixtures.

Furthermore, provided that the acids used are not corrosion-inhibiting themselves, such as the above-mentioned phosphonic acids, and benzoic acid, which is preferably used according to the invention, corrosion inhibitors may be added, in addition to low-temperature stabilizers, enzymes, known antimicrobial active substances, fragrances, dyes, solubilizers, pH correcting agents, salts, and, for production of solid formulations, fillers such as sodium sulfate.

The combination preparations according to the invention may be produced in the form of concentrates, which is advantageous for storage and shipping. In most cases these concentrates have an active substance content of 20 to 40%

or greater. When the concentrates are converted to ready-to-use solutions by adding water or water-alcohol mixtures, the active substance content thereof is adequate for achieving the required microbiocidal effect. Stock solutions are practical for safe and risk-free use in the household.

On account of their bactericidal and mycobactericidal, fungicidal, virucidal, and desired cleaning effect, the systems according to the invention are suited not only for use in the household and the food sector, for which purpose acids may be selected in a targeted manner, which may be either food acids such as citric acid and tartaric acid, or those specifically authorized for foods, but may also be used in appropriate concentrations for instrument and hand disinfection in hospitals, and in industry and agriculture. Use as dermatological agents is also possible.

For use as a disinfectant hand cleanser or dermatological agent, semisolid, i.e., paste-like, cream, or gel preparations may be considered, provided that the alkyl sulfonates and alkyl sulfates used are compatible with the skin, such as the triethanolamine salt of decane sulfate. As acid components, C_8–C_{12} fatty acids which may be straight-chain or branched are used as adjuvants, and depending on the application

form, also organic or inorganic thickeners, emollients, alcohols, fragrances, and ointment bases.

Toxicological studies of the alkyl sulfonates and alkyl sulfates used according to the invention have shown an LD_{50} of 2100 mg/kg for oral administration in mice, which is physiologically safe.

Thus, the invention provides an extremely effective and toxicologically safe disinfectant whose advantages are realized in particular for the food sector and in the household.

The following examples explain the invention:

Example 1

A ready-to-use formulation was prepared from the components listed below:

L(+)-tartaric acid	0.5%
Benzoic acid	1.0
Sodium alkyl sulfonate (mixture with C_{10}–C_{16} chain lengths)	2.0
Ethanol	20.0
Water, permutated	76.5
	100%

Testing of the microbiological activity of this formulation with a pH of 2.65 according to DGHM [Deutsche Gesellschaft für Hygiene und Mikrobiologie (German Society for Hygiene and Microbiology)] gave the following results:

1. Bactericidal activity

(Suspension test; kill time in min.)

Conc., %	Staph.	Coli	Ps. aerug.	Proteus	Klebs.
50	2.5	2.5	2.5	2.5	2.5
10	2.5	2.5	2.5	2.5	2.5
3	2.5	15	2.5	2.5	15
1.5	2.5	>60	5	5	>60

2. Fungicidal activity

(Suspension test; kill time in min.)

Conc., %	Pen. exp.	Asp. niger	Candida albicans
100	2.5	2.5	2.5
50	2.5	2.5	2.5
25	15	5	2.5
10	>60	>60	15

3. Virucidal activity of the formulation according to Example 1 against polio viruses

Time, min.	Titer reduction, $\log_{10}$
5	>8
15	>8
30	>8
60	>8

4. Mycobacterium amegmatis was killed within 60 min. using the formulation from Example 1.

5. Killing of bacteria on PVC and varnished surfaces, using the formulation from Example 1.

a) at room temperature

b) at 277° (+4°C)

The count figures represent the counted bacterial colonies; the first number represents the PVC surface, and the second, the varnished surface.

a)

Bacterium	Action time in minutes			
	5	15	30	60
Staph.	0/0	0/0	0/0	0/0
Klebs.	29/0	0/0	0/0	0/0
E. coli	0/0	0/0	0/0	0/0
Ps. aerug.	0/0	0/0	0/0	0/0
Proteus	0/0	0/0	0/0	0/0

b)

Bacterium	Action time in minutes			
	5	15	30	60
Staph.	0/0	0/0	0/0	0/0
Klebs.	100/17	0/0	0/0	0/0
E. coli	0/0	0/0	0/0	0/0
Ps. aerug.	0/0	0/0	0/0	0/0
Proteus	0/0	0/0	0/0	0/0

6. Killing of fungi on PVC and varnished surfaces, using the formulation from Example 1

a) at room temperature

b) at 277° (+4°C)

The count figures represent the counted bacterial colonies; the first number represents the PVC surface, and the second, the varnished surface.

a) Fungi	Action time in minutes			
	5	15	30	60
Candida alb.	0/0	0/0	0/0	0/0
Pen. expans.	0/0	0/0	0/0	0/0
Asp. niger	0/0	0/0	0/0	0/0
b)				
Candida alb.	0/0	0/0	0/0	0/0
Pen. expans.	27/0	0/0	0/0	0/0
Asp. niger	0/0	0/0	0/0	0/0

Example 2

The following formulation was prepared:

Sodium alkyl sulfonate (C_{10}–C_{16})	3.0%
L(+)-tartaric acid	0.75%
Water, permutated	96.25%
	100.00%

Using this formulation having a pH of 2.7, counting of bacterial colonies in the area test according to DGHM gave the following results:

Table 1

PVC	Varnish	PVC	Varnish	PVC	Varnish	PVC	Varnish
Staph. aureus		Klebsiella		Asp. fumigatus		Asp. niger	
		At room temperature					
5'15'30'60'	5'15'30'60'	5'15'30'60'	5'15'30'60	5'15'30'60'	5'15'30'60'	5'15'30'	5'15'30'6
0 0 0 0	0 0 0 0	0 0 0 0	'			60'	0'
			0 0 0 0 0				
Control	∞	∞	∞	∞	∞	∞	>300
		At 277° (4°C)					
0 0 0 0	0 0 0 0	300	100 <10 <10	100	0 0 0		
Control	∞	∞	∞	∞			

In the suspension test according to DGHM the fungicidal effect of this formulation was not as satisfactory, as shown by the following values:

Concentration, %	Aspergillus fumigatus	Aspergillus niger
100	>60'	>60'
50	>60'	>60'
25	>60'	>60'

However, excellent activity against fungi may be achieved by varying the acid components in the compositions according to the invention, as shown in Example 3 below.

Example 3

The tested formulation had the following composition:

Sodium dodecyl sulfonate	20%
L(+)-tartaric acid	5%
Benzoic acid	5%
Ethanol	15%
Water, permutated	55%
	100%

Table 2

Conc., %	Staph.	Ps. aerug.	Proteus	Klebs.	Trichophyton methagrophyter	Asp. niger	*Cand.* albicans
10	2.5'	2.5'	2.5'	2.5'	2.5'	2.5'	2.5'
5	2.5'	2.5'	2.5'	2.5'	2.5'	2.5'	2.5'
1	2.5'	2.5'	2.5'	2.5'	2.5'	2.5'	2.5'

Example 4

A solid (powdered) formulation was prepared from the following components:

Sodium lauryl sulfonate	10 parts
Sodium decane sulfate	10 "
L(+)-tartaric acid	3 "
Furan-2-carboxylic acid	5 "
Sodium sulfate	72 "

The results for additional formulations according to the invention using the suspension test according to DGHM are presented in Tables 3 through 11. The tables show that comparable results are achieved by using other organic acids besides tartaric and/or benzoic acid, by replacing the sodium salt of the alkyl sulfonates and alkyl sulfates with other salts, by adding alcohols as solubilizer, or by varying the ratio of sulfonate or sulfate to organic acids.

Table 3

Composition	%	pH	Conc. %	Staph. aureus	E. coli	Candida albicans	Ps. aeruginosa	Proteus	Klebsiellae
Monoethanolamine dodecyl sulfate	3.0		10	2.5'	2.5'	2.5'	15'	5'	2.5'
L(+)-tartaric acid	0.75		5	2.5'	2.5'	5'	15'	5'	2.5'
Permutated water	96.25		2	2.5'	60'	15'	15'	5'	30'
			1	2.5'	>60'	30'	>60'	>60'	>60'
Control: Phenol			1%	15'	15'	>60'	2.5'	30'	2.5'

Table 4

Composition	%	pH	Conc. %	Staph. aureus	E. coli	Candida albicans	Ps. aeruginosa	Proteus	Klebsiellae
	%	2.12	100	2.5'	2.5'	2.5'	2.5'	2.5'	2.5'
Sodium alkyl sulfonate	3.0								
C_{10}–C_{16} mixture			25	2.5'	2.5'	5'	2.5'	2.5'	2.5'
Cyclohexanesulfaminic acid	0.90		6.25	2.5'	5'	15'	5'	2.5'	5'
Permutated water	96.10								
Control: Phenol			1%	30'	30'	60'	2.5'	15'	5'

Table 5

Composition	%	pH	Conc., %	Staph. aureus	E. coli	Candida albicans
		2.95	100	2.5'	2.5'	15'
Sodium alkyl sulfate	3.0		50	2.5'	2.5'	15'
C_{10}–C_{16} mixture			25	2.5'	2.5'	15'
1,2-propanediol	5.0		12.5	2.5'	2.5'	15'
L(+)-ascorbic acid	0.88		6.25	2.5'	15'	15'
Permutated water	91.12		3.12	2.5'	>60'	30'
Control: Phenol			1%	15'	15'	60'

Table 6

Composition	%	pH	Conc., %	Staph. aureus	E. coli	Candida albicans
		2.7	100	2.5'	2.5'	15'
Sodium alkyl sulfate	3.0					
C_{10}–C_{16} mixture			12.5	2.5'	2.5'	15'
1,2-propanediol	5.0		6.25	2.5'	5'	30'
Glycolic acid	0.38		3.12	2.5'	15'	30'
Permutated water	91.62		1.56	2.5'	60'	60'
Control: Phenol			1%	30'	60'	60'

Table 7

Composition	%	pH 2.54	Conc., % 100	Staph. aureus 2.5'	E. coli 2.5'	Candida albicans 2.5'
Sodium alkyl sulfonate	3.0					
C_{10}–C_{16} mixture			12.5	2.5'	2.5'	2.5'
1,2-propanediol	5.0		6.25	2.5'	5'	2.5'
Furan-2-carboxylic acid	0.56		3.12	2.5'	5'	2.5'
(benzogalactaric acid)			1.56	2.5'	30'	5'
Permutated water	91.44		0.75	5'	>30'	>30'
Control: Phenol			1%	30'	30'	30'

Table 8

Composition	%	pH	Conc., %	Staph. aureus	E. coli	Candida albicans
		2.18	100	2.5'	2.5'	2.5'
Sodium alkyl sulfonate C_{10}–C_{16} mixture	3.0		50	2.5'	2.5'	5'
1,2-propanediol	5.0		12.5	2.5'	2.5'	5'
Pyruvic acid	0.44		6.25	2.5'	5'	15'
Permutated water	91.56		3.12	2.5'	>60'	15'
Control: Phenol			1%	15'	30'	60'

Table 9

Composition	%	pH	Conc., %	Asp. niger	Pen. expansum
Monoethanolaimne	3.0	2.6	100	2.5'	2.5'
dodecyl sulfate			50	5'	2.5'
Glycolic acid	0.38		25	15'	30'
Benzoic acid	1.0				
Ethanol	20.0				
Permutated water	75.62				

Table 10

Composition	%	pH	Conc., %	Staph. aureus	E. coli	Candida albicans
Alkyl sulfonate mixture	1.0		100	2.5'	2.5'	2.5'
C_8–C_{18}			25	2.5'	2.5'	2.5'
Glycolic acid	7.0		10	2.5'	2.5'	5'
Water	90.0		1.5	2.5'	5'	60'
			0.75	2.5'	60'	60'

Table 11

Composition	%	pH	Conc., %	Staph. aureus	E. coli	Candida albicans
			100	2.5'	2.5'	2.5'
Alkyl sulfonate mixture	9.0					
C_8–C_{18}			25	2.5'	2.5'	15'
Glycolic acid	1.0		5	2.5'	2.5'	15'
Water	90.0		1.5	2.5'	15'	15'
			0.75	2.5'	>60	>60